Newly added claim 12 states that in the method defined in claim 1, the azithromycin is in the form of the dihydrate. Support is at page 3, line 11.

Newly added claim 13 states that in the method defined in claim 1, the ocular infection is trachoma. Support is at page 3, line 5.

Newly added claim 14 states that in the composition defined in claim 5, the azithromycin concentration is from 0.2 to 2.0 weight %. Support is at page 3, line 19. Newly added claim 15 states that the composition defined in claim 4 is suitable for application in a regimen comprising once-a-day topical dosing. Support is at page 2, lines 19-20.

Newly added claim 16 states that in the composition defined in claim 4, the azithromycin is in the form of the dihydrate. Support is at page 3, line 11.

Newly added claim 17 states that the composition defined in claim 4 is suitable for use in treating trachoma. Support is at page 3, line 5.

In the November 17, 2000 Office Action, claims 4-6 and 9 were rejected under 35 USC 102(b) or, in the alternative, under 35 USC 103(a) as obvious over Bailey et al or Thylefors for the reasons set forth in the previous Office Action (i.e., of April 11, 2000). In the 11/17/00 Office Action, the Examiner stated, in pertinent part:

> Applicant's arguments filed October 16, 2000 have been fully considered but they are not persuasive.
>
> It is noted that Bailey and Thylefors do not disclose applying azithromycin topically to the eye. Therefore, applicant's arguments have been found persuasive with respect to the method claims. However, the instant composition claims 4-6 and 9 encompass nothing more than an old compound in water. Therefore, the claimed compositions are not patentable over the art of record. (Office Action, page 2).

The rejection is traversed on the basis that Bailey or Thylefors simply do not provide a basis for it, particularly in light of the claims as now amended. Both references are directed to the administration of azithromycin by a route which is clearly systemic (i.e., oral). Bailey states, in the summary (first sentence of the second paragraph):

> We carried out a randomised single-blind comparison of azithromycin (a single **oral** dose of 20 mg/kg) with conventional treatment (6 weeks of topical tetracycline plus erythromycin for severe cases) in two villages with endemic trachoma in The Gambia.

Similarly, Thylefors contains no statement which would indicate that azithromycin should be given by any route other than oral, as evidenced by his statement to the effect that:

> Furthermore, azithromycin has particular pharmacokinetic properties; it is rapidly and widely distributed throughout the body, and it shows markedly high concentrations in tissue as compared to plasma. (Thylefors, page 133, last paragraph of left column)

Clearly, by his reference to the wide distribution of azithromycin throughout the body, Thylefors is concerned with systemic administration. Neither Bailey nor Thylefors suggests topical application to the eye. As such, neither comes even close to suggesting azithromycin in a topical ocular formulation which is in the form of an ointment, gel, or an ophthalmic solution in isotonic saline, as independent claim 4 now requires. Amended claim 4 also patentably distinguishes over azithromycin in water, and thus clearly obviates the comment made by the Examiner.

It is further noted that, in order for obviousness to lie, the prior art must not only contain a suggestion of the invention, but must also contain a reasonable expectation of success. . Both the suggestion of an invention and an expectation of success must be based in the prior art. American Hospital supply Corp. v. Travenol Laboratories, Inc., 223 USPQ 577, 582 (Fed. Cir. 1984). The Federal Circuit has explained the proper test:

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out **and would have a reasonable likelihood of success**, viewed in light of the prior art. **Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure** (emphasis added).

In re Dow Chemical Co., 5 USPQ.2d 1529, 1531 (Fed. Cir. 1988); Amgen, Inc. V. Chugai Pharmaceutical Co. Ltd. 18 USPQ.2d 1016. 1022-23 (Fed. Cir.), cert. denied 502 U.S. 856 (1991). Here, neither Thylefors nor Bailey even remotely provides a suggestion of Applicant's compositions as now claimed, much less any expectation of success. Indeed, neither could provide any expectation of success since neither is concerned with the topical ocular application of azithromycin. Thus, the Examiner is respectfully urged to reconsider her position in light of the claims as now amended, and to withdraw the rejection over Bailey and Thylefors.

Claims 1-6 and 8-9 stand rejected under 35 USC 102(a) as anticipated by or, in the alternative, under 35 USC 103(a) as obvious over First Meeting of the WHO Alliance For The Global elimination of Trachoma (hereinafter "WHO"), Geneva, 30 June – 1 July 1997, for the reasons set forth in the Office Action of April 11, 2000.

Applicants' acknowledge the reasoning the Examiner set forth in the Office Action in support of the rejection over WHO, although Applicants do not necessarily agree with that reasoning. In any case, it is believed that the rejection is overcome by virtue of the Declaration under Rule 131 of Imran Ahmed, the inventor, which Declaration is submitted herewith. By means of the enclosed Declaration, WHO is antedated and removed as a reference against this application, and it is respectfully requested that the rejection be withdrawn.

In the Declaration, the inventor states that, in a rabbit model, he tested a topically applied ocular composition comprising 0.5 % azithromycin dihydrate dispersed into a commercially obtained, sterile ointment vehicle (Tearfair™). The active azithromycin composition was tested against a placebo control, with azithromycin topical ocular composition being instilled into the left eye and placebo into the right eye in each animal.

After conducting the rabbit study, the inventor co-authored a memorandum which summarized the study's results. A page from that memo bearing "Table 2" is attached to the Declaration as Exhibit 1. The Table summarizes individual tissue concentrations (μg azithromycin/g tissue) in the eye of each rabbit following the instillation of a single dose of azithromycin ophthalmic ointment or placebo.

The memorandum was acknowledged and "signed off" as either having been authored, reviewed and approved, or approved for distribution by a number of scientists and/or employees within Pfizer, in addition to the inventor. This is demonstrated by page 3 from the memorandum on which the signatures appear. A copy of page 3 is attached to the Declaration as Exhibit 2. Page 3 also evidences the conclusions from the rabbit study conducted by the inventor, definitively demonstrating that a topical ocular formulation and the corresponding method of topically applying the topical azithromycin ocular ointment to the eye were reduced to practice.

The study and the memorandum described in the Declaration were, respectively, conducted and written and issued prior to 30 June-1 July, 1997, the date of the WHO reference. The WHO article is accordingly antedated and removed as a reference.

For the record, it is noted that a third party approached Pfizer with an inquiry about azithromycin in a topical formulation for use in the eye, as evidenced by a letter received within Pfizer which is attached to the Declaration as Exhibit 3. The inventor has additionally stated in the Declaration that the rabbit study he conducted and the resulting memo he co-authored occurred prior to this third party contact with Pfizer regarding the ocular administration of azithromycin, including prior to the date of Exhibit 3.

Thus, it is respectfully submitted that the evidence provided by the Declaration proves conclusively that Dr. Ahmed made his invention prior to WHO and prior to the third party contact made with Pfizer.

In view of the foregoing comments and amendments, this case is believed to be in condition for allowance, and a Notice of Allowance is courteously solicited.

Respectfully submitted,

November 12, 2001
Date

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VERSION MARKED UP TO SHOW CHANGES MADE

Claim 4 has been amended as follows:

4. (Twice amended) A composition for topical application directly to an eye of an animal,

said composition being suitable for the treatment of an ocular infection,

said composition comprising an effective amount of azithromycin in a pharmaceutical vehicle suitable for topical application to the eye, and

said composition being in the form of an ointment, gel or an ophthalmic solution in isotonic saline,

The following new claims have been added

:

10. A method as defined in claim 2, wherein said azithromycin concentration is from 0.2 to 2.0 weight %.

11. A method as defined in claim 10, wherein said azithromycin concentration is 0.5 weight %.

12. A method as defined in claim 1, wherein said azithromycin is in the form of the dihydrate.

13. A method as defined in claim 1, wherein said ocular infection is trachoma.

14. A composition as defined in claim 5, wherein said azithromycin concentration is from 0.2 to 2.0 weight %.

15. A composition as defined in claim 4, wherein said composition is suitable for application in a regimen comprising once-a-day topical dosing.

16. A composition as defined in claim 4, wherein said azithromycin is in the form of the dihydrate.

17. A composition as defined in claim 4, wherein said ocular infection is trachoma.